CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Neurology – Qalsody Utilization Management Medical Policy
- Qalsody® (tofersen intrathecal injection – Biogen)

REVIEW DATE: 03/25/2026

OVERVIEW

Qalsody, an antisense oligonucleotide, is indicated for the treatment of **amyotrophic lateral sclerosis (ALS)** in adults who have a mutation in the **superoxide dismutase 1 (*SOD1*) gene**.[1]

This indication is approved under accelerated approval based on reduction in plasma neurofilament light chain observed in patients treated with Qalsody. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

Clinical Efficacy

Clinical efficacy of Qalsody was evaluated in the Phase III, randomized (2:1), placebo-controlled VALOR study (n = 108) and open-label extension (OLE) [n = 95].[2,3] Patients were adults with weakness attributable to ALS and a confirmed *SOD1* pathogenic variant.[2] Enrollees were subdivided into "faster-progression" and "slower-progression" subgroups based on predefined criteria; this delineation was intended to enrich the evaluable population for clinical endpoints over the 6-month trial period. Clinical endpoints were not formally tested in the slower-progressing subgroup. Although statistical significance was not reached for clinical endpoints in the VALOR study, change in plasma neurofilament light chain (NfL) at Week 28 was also assessed in the total population (faster- and slower-progressing subgroups) as a secondary endpoint; there was a 55% reduction from baseline in NfL with Qalsody-treated patients vs. a 12% increase with placebo-treated patients.[1,2] Of note, similar findings were observed among the faster-progression and slower-progression subgroups.

After completion of VALOR, 95 patients continued into the VALOR OLE.[2,3] Week 52 data were published along with the primary VALOR analysis (January 2022 data cutoff)[2]; final data were later published (August 2024 data cutoff) after all patients had the opportunity for a Week 192 post-VALOR visit.[3] Treatment effects were analyzed according to "early start" (received Qalsody during randomized phase) vs. "delayed start" (received placebo during randomized phase) cohorts.[2,3] Both the early-start and delayed-start Qalsody groups experienced substantial decline in plasma NfL levels; maximum reduction was observed by approximately 16 weeks and sustained over time (Week 148: 67% vs. 64% reductions for early- and delayed-start Qalsody, respectively). Favorable trends in clinical endpoints were also observed for early- vs. delayed-start Qalsody recipients; however, the OLE was not designed to evaluate statistical significance of these endpoints.

Neurofilament Light Chain (NfL)

NfL is an intermediate filament uniquely expressed in neurons.[4] When axons are injured or degenerating, NfL leaks into the interstitial fluid before passing into the cerebrospinal fluid and blood where levels can be quantified.[5] Several nonrandomized studies have demonstrated that NfL levels correlate with disease severity, disease progression rate, and survival.[5-13] These studies have confirmed that NfL levels are positively correlated with disease progression and higher NfL levels indicate a shorter survival period. Higher levels of NfL are associated with greater and faster decline on ALS Functional Rating Scale – Revised (ALSFRS-R) score over time.[6] Higher levels are also associated with higher risk of unfavorable clinical outcomes, such as death, tracheostomy, and/or permanent ventilation.[5]

Guidelines

The European Academy of Neurology, in collaboration with European Reference Network for Neuromuscular Diseases (2024), recommends Qalsody as first-line treatment in patients with progressive ALS caused by pathogenic variants in *SOD1*.[14] This treatment should be discussed with patients as it may be associated with serious adverse events. In patients with slow progression, it is important to discuss the balance of potential benefits and harms. Qalsody is not addressed in earlier guidelines (e.g., those from the American Academy of Neurology).[15,16]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Qalsody. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Qalsody as well as the monitoring required for adverse events and long-term efficacy, approval requires Qalsody to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Qalsody is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Amyotrophic Lateral Sclerosis (ALS).** Approve for 6 months if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has a confirmed *SOD1* pathogenic variant; AND
     - **iii.** Patient has weakness attributable to ALS; AND
     - **iv.** According to the prescriber, the patient has adequate respiratory function and does not require invasive ventilation; AND
     - **v.** The medication is prescribed by or in consultation with a neurologist, a neuromuscular disease specialist, or a physician specializing in the treatment of ALS; OR
   - **B)** Patient is Currently Receiving Qalsody. Approve if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient has a confirmed *SOD1* pathogenic variant; AND
     - **ii.** According to the prescriber, the patient continues to derive benefit from therapy; AND
     - **iii.** Patient does not require invasive ventilation; AND
     - **iv.** The medication is prescribed by or in consultation with a neurologist, a neuromuscular disease specialist, or a physician specializing in the treatment of ALS.

   Dosing. Approve the following dosing regimens (A and B):

A) 100 mg (15 mL) administered intrathecally not more frequently than once every 14 days for 3 doses; AND
B) 100 mg (15 mL) administered intrathecally not more frequently than once every 28 days.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Qalsody is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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13. Lu CH, Macdonald-Wallis C, Gray E, et al. Neurofilament light chain, a prognostic biomarker in amyotrophic lateral sclerosis. *Neurology*. 2015;84:2247-2257.
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15. Miller RG, Jackson CE, Kasarskis EJ, et al. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: multidisciplinary care, symptom management, and cognitive/behavioral impairment (an evidence-based review). *Neurology*. 2009 (reaffirmed 2023);73(15):1227-1233.
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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	06/19/2024
Annual Revision	No criteria changes.	06/18/2025
Early Annual Revision	**Policy Statement:** The Policy Statement was updated to reflect that Amyotrophic Lateral Sclerosis (ALS) was added as a new condition of approval. **Amyotrophic Lateral Sclerosis (ALS):** This coverage condition was moved from Conditions Not Recommended for Approval to FDA-Approved Indication; coverage requirements were added to the policy.	03/25/2026